

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

1. (Currently Amended) A modified antibody of class IgG with FcRn binding affinity altered relative to that of an unmodified antibody, comprising a heavy chain variable region and a heavy chain constant region wherein at least amino acid residues 250 and 428, EU numbering, are different from the residues present in the unmodified human class IgG antibody.
2. (Original) The modified antibody according to Claim 1, wherein said unmodified class IgG antibody comprises a heavy chain constant region of a human IgG1, IgG2, IgG2M3, IgG3 or IgG4 molecule.
3. (Original) The modified antibody according to Claim 1, wherein said unmodified class IgG antibody comprises a heavy chain constant region of a human IgG1 or IgG2M3 molecule.
4. (Canceled)
5. (Currently amended) The modified antibody according to ~~Claim 1~~ Claim 2, wherein said unmodified class IgG antibody is a human class IgG1 antibody.
6. (Currently amended) The modified antibody according to Claim 1, wherein the unmodified antibody is OST577-IgG2M3, with a heavy chain variable region, a heavy chain constant region, a light chain variable region, and a light chain constant region represented by SEQ ID NOs: 1, 2, 4, and 5, respectively, or OST577-IgG1, with a heavy chain variable region, a heavy chain constant region, a light chain variable region, and a light chain constant region represented by SEQ ID NOs: 1, 3, 4, and 5, respectively.

7. (Canceled)

8. (Currently amended) ~~[[The]]~~ A modified antibody according to Claim 1, of class IgG with FcRn binding affinity altered relative to that of an unmodified antibody, comprising a heavy chain constant region wherein:

(a) ~~said~~ amino acid residue 250, EU numbering, from the heavy chain constant region is glutamic acid or glutamine; or

(b) ~~said~~ amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine or leucine.

9. (Currently amended) The modified antibody according to Claim 1, wherein amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine.

10. (Currently amended) The modified antibody according to Claim 1, wherein amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

11. (Currently amended) ~~[[The]]~~ A modified antibody according to Claim 1, of class IgG with FcRn binding affinity altered relative to that of an unmodified antibody, comprising a heavy chain constant region wherein:

(a) ~~said~~ amino acid residue 250, EU numbering, from the heavy chain constant region is glutamic acid and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine;

(b) ~~said~~ amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine; or

(c) ~~said~~ amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

12. (Currently amended) The modified antibody according to Claim 1, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

13. (Canceled)

14. (Canceled)

15. (Currently amended) ~~[[The]]~~ A modified antibody according to Claim 1, of class IgG with FcRn binding affinity altered relative to that of an unmodified antibody, comprising a heavy chain constant region wherein:

(a) ~~said~~ amino acid residue 250, EU numbering, from the heavy chain constant region is selected from the group consisting of arginine, asparagine, aspartic acid, lysine, phenylalanine, proline, tryptophan, or tyrosine; or

(b) ~~said~~ amino acid residue 428, EU numbering, from the heavy chain constant region is selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, proline, serine, threonine, tyrosine, or valine.

16. (Currently amended) The modified antibody according to Claim 15, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is aspartic acid.

17. (Currently amended) The modified antibody according to Claim 15, wherein said amino acid residue 428, EU numbering, from the heavy chain constant region is glycine.

18. (Original) The modified antibody according to Claim 1, wherein the modified antibody has a higher binding affinity for FcRn at pH 6.0 than at pH 7.4.

19. (Currently Amended) An antibody comprising a heavy chain variable region and a heavy chain constant region substantially identical to that of a naturally occurring class IgG antibody, wherein at least the heavy chain constant region amino acid residues 250 and 428, EU numbering, are different from the residues present in the naturally occurring class IgG antibody, and wherein the *in vivo* serum half-life of said antibody is increased relative to the naturally occurring antibody.

20. (Original) The antibody according to Claim 19, wherein said naturally occurring class IgG antibody comprises a heavy chain constant region of a human IgG1, IgG2, IgG2M3, IgG3 or IgG4 molecule.

21. (Original) The antibody according to Claim 19, wherein said naturally occurring class IgG antibody comprises a heavy chain constant region of a human IgG1 or IgG2M3 molecule.

22. (Canceled)

23. (Original) The antibody according to ~~Claim 19~~ Claim 20 wherein said naturally occurring class IgG antibody is a human class IgG1 antibody.

24. (Currently amended) ~~[[The modified]]~~ An antibody according to Claim 19, comprising a constant region substantially identical to that of a naturally occurring class IgG antibody wherein:

(a) said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamic acid or glutamine; or

(b) said amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine or leucine; and

wherein the *in vivo* serum half-life of said antibody is increased relative to the naturally occurring antibody.

25. (Currently amended) The antibody according to Claim 19, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine.

26. (Currently amended) The antibody according to Claim 19, wherein said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

27. (Currently amended) ~~[[The modified]]~~ An antibody according to Claim 19, comprising a constant region substantially identical to that of a naturally occurring class IgG antibody wherein:

(a) ~~said~~ amino acid residue 250, EU numbering, from the heavy chain constant region is glutamic acid and said amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine;

(b) ~~said~~ amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine; or

(c) ~~said~~ amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine; and

wherein the *in vivo* serum half-life of said antibody is increased relative to the naturally occurring antibody.

28. (Original) The antibody according to Claim 19, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

29. (Canceled)

30. (Canceled)

31. (Currently amended) ~~[[The modified]]~~ An antibody according to Claim 19, comprising a constant region substantially identical to that of a naturally occurring class IgG antibody wherein:

(a) ~~said~~ amino acid residue 250, EU numbering, from the heavy chain constant region is selected from the group consisting of arginine, asparagine, aspartic acid, lysine, phenylalanine, proline, tryptophan, or tyrosine; or

(b) ~~said~~ amino acid residue 428, EU numbering, from the heavy chain constant region is selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, proline, serine, threonine, tyrosine, or valine; and

wherein the *in vivo* serum half-life of said antibody is increased relative to the naturally occurring antibody.

32. (Currently amended) The antibody according to ~~Claim 19~~ Claim 31, wherein said amino acid residue 250 from the heavy chain constant region is aspartic acid.

33. (Currently amended) The antibody according to ~~Claim 19~~ Claim 31, wherein said amino acid residue 428 from the heavy chain constant region is glycine.

34. (Currently Amended) A modified antibody of class IgG, and comprising a heavy chain variable region and a heavy chain constant region, with an *in vivo* mean elimination half-life at least about 1.8-fold longer than that of the corresponding unmodified class IgG antibody.

35. (Currently Amended) The modified antibody of class IgG of Claim 34, wherein at least one of the heavy chain constant region amino acid residues 250 or 428, EU numbering, is different from that present in the unmodified antibody.

36. (Currently amended) ~~[[The]]~~ A modified therapeutic or diagnostic antibody of class IgG of Claim 34 with an *in vivo* mean elimination half-life at least about 1.8-fold longer than that of the corresponding unmodified class IgG antibody, wherein:

(a) ~~said~~ amino acid residue 250, EU numbering, from the heavy chain constant region is glutamic acid and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine;

(b) ~~said~~ amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine; or

(c) ~~said~~ amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

37. (Currently amended) The modified antibody of Claim 34, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

38. (Currently amended) The modified antibody of Claim 34, wherein amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

39. (Currently Amended) A modified antibody of class IgG, and comprising a heavy chain variable region and a heavy chain constant region, with an *in vivo* mean serum clearance rate at least about 1.8-fold lower than that of the corresponding unmodified class IgG antibody.

40. (Currently Amended) The modified antibody of class IgG of Claim 39, wherein at least one of ~~[[ef]]~~ the heavy chain constant region amino acid residues 250 or 428, EU numbering, is different from that present in the unmodified class IgG antibody.

41. (Currently Amended) ~~[[The]]~~ A modified antibody of class IgG of Claim 39, with an *in vivo* mean serum clearance rate at least about 1.8-fold lower than that of the corresponding unmodified class IgG antibody wherein

(a) ~~said~~ amino acid residue 250, EU numbering, from the heavy chain constant region is glutamic acid and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine;

(b) ~~said~~ amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine; or

(c) ~~said~~ amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

42. (Currently amended) The modified antibody of Claim 39, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

43. (Currently amended) The modified antibody of Claim 39, wherein said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

44. (Canceled)

45. (Canceled)

46. (Canceled)

47. (Canceled)

48. (Canceled)

49. (Currently amended) A modified antibody of class IgG, and comprising a heavy chain variable region and a heavy chain constant region, derived from an unmodified antibody of class IgG wherein residue 250, EU numbering, from the heavy chain constant region is alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine,



histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, tryptophan, tyrosine, or valine.

50. (Canceled)

51. (Canceled)

52. (Currently amended) An antibody fragment comprising a heavy chain constant region or a heavy chain Fc region of the modified antibody according to ~~Claim 1~~ Claim 2.

53. (Currently amended) An antibody fragment comprising a heavy chain constant region or a heavy chain Fc region of the antibody having a constant region substantially identical to that of a naturally occurring class IgG antibody according to ~~Claim 19~~ Claim 20.

54. (Withdrawn) A polypeptide comprising an amino acid sequence of anyone of SEQ ID NOs: 10-76.

55. (Canceled)

56. (Canceled)

57. (Currently Amended) A method for ~~altering FcRn binding affinity and/or serum half life of an antibody of class IgG~~ preparing an antibody of Claim 1, said method comprising selecting at least two amino acid residues from the heavy chain constant region from the group consisting of residues 250, and 428 and substituting the selected residue(s) residues 250 and 428, EU numbering, in the heavy chain constant region with [[an]] amino acids different from that those present in the unmodified antibody, thereby altering FcRn binding affinity and/or serum half life of the antibody.

58. (Currently Amended) A method of producing a modified antibody of class IgG, and comprising a heavy chain variable region and a heavy chain constant region, with an altered binding affinity for FcRn and/or an altered serum half-life as compared with the unmodified antibody, said method comprising:

- (a) preparing an expression vector comprising a suitable promoter operably linked to DNA encoding at least a variable region and a constant region of an immunoglobulin heavy chain in which ~~at least two amino acid residues from the heavy chain constant region selected from the group consisting of amino acid residues 250, 250 and 428, EU numbering, [[is]]~~ are substituted with a residue different from that present in an unmodified antibody;
- (b) transforming host cells with said vector; and
- (c) culturing said transformed host cells to produce said modified antibody.

59. (Original) The method according to Claim 58, further comprising: preparing a second expression vector comprising a promoter operably linked to DNA encoding a complementary immunoglobulin light chain and further transforming said host cells with said second expression vector.

60. (Currently amended) The method according to Claim 58, wherein:

- (a) said amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with glutamic acid or glutamine; or
- (b) said amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with phenylalanine or leucine.

61. (Currently amended) The method according to Claim 58, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with glutamine.

62. (Currently amended) The method according to Claim 58, wherein said amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with leucine.

63. (Currently amended) The method according to Claim 58, wherein

(a) said amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with glutamic acid and amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with phenylalanine;

(b) said amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with phenylalanine; or

(c) said amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with leucine.

64. (Currently amended) The method according to Claim 58, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with leucine.

65. (Canceled)

66. (Canceled)

67. (Currently amended) The method according to Claim 58, wherein:

(a) amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with a residue selected from a group consisting of arginine, asparagine, aspartic acid, lysine, phenylalanine, proline, tryptophan, or tyrosine; or

(b) amino acid residue 428, EU numbering, is substituted with a residue selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, proline, serine, threonine, tyrosine, or valine.

68. (Currently amended) The method according to Claim 58, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with aspartic acid.

69. (Currently amended) The method according to Claim 58, wherein said amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with glycine.